

**FURTHER EXPERIENCES WITH THE COMPLEMENT FIXATION
TEST IN THE DIAGNOSIS OF GONOCOCCUS INFEC-
TIONS OF THE GENITO-URINARY TRACT IN
THE MALE AND FEMALE.¹**

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In a previous paper² attention was drawn to the value of the serum diagnosis of gonococcus infections in general. We there showed that in chronic gonococcus infection, even though limited to the genito-urinary tract, an antibody specific for the gonococcus could readily be detected in the blood. Our experimental work showed that the secret of success lay in the use of a polyvalent antigen, on account of the fact that the different strains of the gonococcus seemed to differ considerably one from the other.

We then gave the results of the application of the test to a total of 324 human sera. These results showed that the complement fixation test (using a polyvalent antigen) for gonococcus antibodies should prove an addition to our methods of diagnosing between the various chronic conditions arising from gonococcus infection and similar conditions due to other causes. In addition we pointed out that the complement fixation test might be a distinct aid in finally deciding as to whether a patient was cured of his or her gonococcus infection, inasmuch as the blood test was positive in a certain percentage of cases where other means of diagnosis failed.

Finally, we stated that, in our opinion, the facts at hand seemed to prove conclusively that a positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

Since then articles by Swinburne,³ Keyes,⁴ Schmidt,⁵ and Gradwohl⁶ have appeared corroborating our results in all essential particulars.

TECHNIQUE. The antigen used at the present time is prepared as follows: The various strains of gonococci are grown on salt-free

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² AMER. JOUR. MED. SCI., May, 1911.

³ Arch. of Diag., July, 1911.

⁴ AMER. JOUR. MED. SCI., Jan., 1912.

⁵ Trans. Amer. Urol. Assoc., 1911.

⁶ Amer. Jour. Derm. and Syph., Urinary Diseases, June, 1912.

veal agar, neutral in reaction to phenolphthalein; twenty-four-hour old cultures are washed off the agar slants with distilled water and the resulting suspension is heated for two hours in the water-bath at 56° C. It is then centrifugated and passed through a Berkefeld filter. No salt is added to this antigen until it is desired to use it, when it is made up to 0.9 per cent. strength by adding one part of 9 per cent. saline solution to nine parts of antigen.

The antigen is best preserved in small quantities in sealed tubes, heated to 56° C. for half an hour on three successive days, to insure sterility. If possible, the antigen is standardized with a known positive serum from a clinical case. If this is impossible, immune rabbit serum may be used, provided that the minimum amount of the serum which will completely fix complement is used. An antigen titrated with a highly immune rabbit serum may show perfect fixation in an amount that would fail to show any fixation with the average clinical case, on account of the lower antibody content of the latter. Antigens prepared as above will keep almost indefinitely if kept in sealed tubes free from contamination. We now use only the antishoop hemolytic system, but in other respects the technique is the same as described in our previous paper, except that we now use all the ingredients in one-tenth the quantity used in the original Wassermann technique for syphilis.

We may say that for the last few months we have used the gonococcus antigen prepared by Parke, Davis & Co., along with our own, and so far it has given satisfactory results.

SIGNIFICANCE OF A POSITIVE AND A NEGATIVE REACTION. As already stated, we found a positive reaction to be specific for the gonococcus with the sole exception of meningococcus infection.

Our positive results in meningococcus infection were obtained when using a highly immune anti-meningococcus serum prepared according to Flexner's method. We have since tested the serum of several patients suffering from cerebrospinal meningitis, with uniformly negative results. It would, therefore seem that, clinically, the complement fixation test for gonococcus infection is absolutely specific for the gonococcus. As is well known, the Wassermann reaction is not absolutely specific for syphilis. A positive reaction is obtained in various other diseases, notably leprosy, chronic malaria, frambesia, etc., probably due to the fact that the serum in these diseases contains abundant lipotropic substances. In the gonococcus complement fixation test we have a true antigen-antibody combination, inasmuch as the antigen is prepared from the specific infecting organism of the disease in question. In the Wassermann reaction we do not have this true antigen-antibody combination. The so-called antigens in the Wassermann reaction are present in the lipoidal substances of the tissues whether derived from luetic or non-luetic human subjects or animals. This probably accounts for the superior specificity of the gonococcus complement fixation test.

A negative reaction does not, of course, exclude the possibility of gonococcus infection being present, in the same way as a negative Wassermann reaction does not exclude the possibility of syphilitic infection. In this connection, however, there are two facts to be taken into consideration:

1. In the late lesions of syphilis, in common with the other infectious granulomas, there is a distinct tendency to the formation of a more or less well-marked connective-tissue capsule surrounding the lesion. As a result, there is arrested activity on the part of the spirochetæ, a less amount of toxin is elaborated, the connective-tissue capsule offers some resistance to the free absorption of toxins, and, as a result, there may be lessened antibody formation. This condition does not obtain in gonococcus infection, as the lesions here do not tend to become encapsulated.

2. The Wassermann reaction is definitely obscured by recent mercurial treatment. There is no treatment which thus obscures the complement fixation test for gonococcus infections. On account of these two facts we think that more importance may perhaps be attached to a negative reaction in testing for gonococcus infection than is to be attached to a negative Wassermann test for syphilis.

TIME OF APPEARANCE OF A POSITIVE REACTION. A positive reaction is not to be expected earlier than about the fourth week of the disease, and then only in acute cases with some complication such as acute prostatitis, gonococcus arthritis, etc. For example, in one case of acute gonococcus arthritis coming on three or four days after the onset of the urethritis the blood was negative (though very slowly) on the twenty-first day, and strongly positive on the twenty-eighth day from the first appearance of the urethral discharge. In another similar case the blood was negative on the seventeenth day and strongly positive on the twenty-fifth day of the disease.

TIME OF DISAPPEARANCE OF A POSITIVE REACTION AFTER CURE. It is, of course, evident that the antibodies must persist in the blood for some time after the patient is actually cured. How long they persist is a difficult question to answer precisely. That they do not persist indefinitely we are quite certain. Torrey⁷ has shown that the complement fixatives in the blood of a rabbit immunized to the gonococcus begin to be eliminated ten days after the date of the last inoculation and continue to be eliminated rapidly from the tenth to the fiftieth day, after which they are only found in small quantities.

Our own experiments with rabbits confirm these results. After the fiftieth day from the date of the last inoculation only a reaction can be obtained. This is a reaction to which we attach no importance.

⁷ Jour. Med. Research, 1910, No. 1, p. 95.

Clinically, we have seen one case in which a two-plus reaction changed to a negative in five weeks after cure. The majority of cases, however, take somewhat longer. As a rule, we think a negative reaction should be obtained seven or eight weeks after cure. In other words, if a positive reaction is obtained seven or eight weeks after clinical cure we think that the patient should be looked upon as still harboring gonococci.

RELATIVE VALUE OF THE COMPLEMENT FIXATION AND BACTERIOLOGICAL METHODS OF DIAGNOSIS IN CHRONIC AND DOUBTFUL CASES, AND THE TECHNICAL DIFFICULTIES CONNECTED WITH THE TWO METHODS. As we have already stated, the complement fixation test is specific for the gonococcus. A positive reaction must therefore be looked upon as absolute proof of a focus of gonococcus infection somewhere in the body. What constitutes absolute proof of the gonococcus bacteriologically? Certainly not a smear stained with methylene blue. A Gram stain, properly made, can be accepted where the gonococci are abundant; but in chronic cases, with few organisms present, it cannot be accepted as absolute proof. Among the sources of error may be mentioned the *Micrococcus catarrhalis*; degeneration forms of Gram-positive cocci which not infrequently do not retain the Gram stain, and according to Adami⁸ the *Trichomonas vaginalis* and some aberrant forms of the *Bacillus coli*. All authorities are agreed that in doubtful cases culture methods constitute the only absolute proof.

There is little doubt that the technique of isolating the gonococcus in culture is far more difficult than the technique of a complement fixation test. In the first place, the bacteriologist may err, as Dr. E. L. Keyes, Jr.,⁹ well says, "through his own fault or through the fault of the clinician who submits the specimen to him, and the precision of his diagnosis depends upon a well-prepared specimen as much as upon his own skill." The prostate and vesicles must be thoroughly massaged and the specimen must be fresh, as it is probable that the gonococcus cannot be cultivated if allowed to stand in cool urine for half an hour. In addition, the gonococcus grows only on special media, and culture may fail on account of the presence of other rapidly growing organisms which either inhibit the growth of the gonococcus or render its isolation impossible. This is especially the case in women.

In connection with the complement fixation test, the only real difficulty lies in obtaining and carrying the various strains of the gonococcus necessary for the preparation of a good antigen. Apart from this, if the serologist carefully and frequently titrates the various reagents used in the test, a matter neither difficult nor time-consuming, the technique of the complement fixation test is comparatively simple.

All the above facts must be taken into consideration in judging

⁸ Principles of Pathology, ii, 752.

⁹ Loc. cit.

as to the relative value of the bacteriological and complement fixation methods of diagnosis. In the presence of a positive complement fixation test and negative bacteriological findings, we think the fixation test should be accorded its full value. In the presence of a negative complement fixation test and positive bacteriological findings, we think the bacteriological findings should be accepted as correct only if the proof is absolute—namely, isolation of the gonococcus in culture.

In connection with the above statements the limitations of the complement fixation test, to be detailed later, are, of course, to be borne in mind. In all cases we think that in the interests of the patient both methods of diagnosis should be used.

I. GONORRHEAL URETHRITIS, GONOCOCCI PRESENT.

No. of cases.	Duration.	Reaction.
3	2 weeks	—
4	3 weeks, both urines cloudy	+
1	4 weeks, both urines cloudy	+
1	4 weeks, marked prostatic involvement	+++
2	4 weeks, gonococcus arthritis, 3 weeks	+++
1	5 weeks, both urines cloudy	+
2	6 weeks, both urines cloudy	+
1	7 weeks, prostatic abscess	++
2	8 weeks, both urines cloudy	++
1	8 weeks, prostatic involvement	++
1	8 weeks, second urine clean	—
1	10 weeks, second urine clean	—
4	12 weeks, prostatic involvement	+++

Remarks. The above illustrates the gradual development of a positive reaction.

In anterior urethritis, whether acute or chronic, a positive reaction is not obtained. Cases of urethritis remaining confined to the anterior urethra are, of course, rare. Most authorities agree that in the great majority of cases the posterior urethra is involved. One of Dr. Keyes' cases, however, had had urethritis for ten weeks. The first urine passed was slightly cloudy, the second urine, passed after the prostatic massage was quite clear and microscopic examination revealed no gonococci. There was a thin mucoid discharge at the meatus, in which gonococci were found, and they were also obtained in culture. Culture made from the urine passed after the prostatic massage was sterile. Here the infection was probably confined to a few glands in the fossa navicularis and there was not enough absorption of toxins to stimulate antibody formation. This case is cited here in order to bring out the point that probably a positive reaction is never found when the disease remains confined to the anterior urethra.

A weakly positive (one-plus) reaction first makes its appearance in the third week of the disease and only then when the posterior urethra is affected. In the ordinary case of acute antero-

posterior urethritis without complications running on to cure in six to eight weeks, the most that can be expected is a one-plus reaction. In the absence of complications a strong positive (two-plus) reaction does not make its appearance until the disease has lasted about eight weeks. A two-plus or three-plus reaction can be obtained as early as the fourth week, when there is some definite complication such as acute prostatitis, arthritis, etc. In fact, a three-plus reaction probably is not found when the disease is limited to the genito-urinary tract unless there is some definite implication of the deeper structure.

The fact that a positive reaction is not obtained in the early weeks of the infection, should prove an aid in differentiating between a fresh infection and the recurrence of an old, apparently cured, one. This also suggests possible medico-legal application of the test. Case XXI of Dr. Keyes¹³ series, illustrates this point. This was a married man who had infected his wife with gonorrhea some months previously. Both were treated and finally declared cured, and the blood test made some months later was negative in both. Two weeks later he returned, absolutely denying extramarital exposure, but with a fresh gonorrhea two weeks old. Both he and his wife had the blood test made again, and both were negative. Four weeks later he was positive and she was negative, and she remained clinically cured. As Dr. Keyes says: "The development of a positive reaction in him showed the infection to be a fresh one due to extramarital exposure, in spite of his fervent denials." Dr. Keyes informs us that some six months later the husband finally confessed to the truth of the preceding statement.

Undoubtedly, however, the cases of greatest importance to the clinician, especially when the question of marriage arises, are those of chronic urethritis, prostatitis, and seminal vesiculitis following gonorrhea. Prostatitis is probably the most frequent and important complication. In many such cases we have obtained a positive complement fixation test when bacteriological methods have left us in doubt as to the presence or absence of the gonococcus. It is in such cases that we think the complement fixation test will prove an addition to bacteriological examination.

II. CHRONIC ANTEROPOSTERIOR URETHRITIS.

1. *Gonococci present:* In our experience in these cases a positive reaction is practically constantly found and we do not propose to enter into any detail here. We can only recall one case out of a great many examined in which the complement fixation test failed. This was a case of urethritis, followed in a few days by a multiple gonococcus arthritis. The blood was negative on the thirteenth, twenty-sixth, and thirty-sixth days of the disease,

¹³ Loc. cit.

and positive on the sixty-first day. By that time, however, the patient had received eight injections of gonococcus vaccine which would have rendered the reaction positive in any case.

2. Gonococci doubtful: This group includes 5 cases in which both smear and cultural examinations were made, but in which the findings were inconclusive.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows fairly abundant sediment of pus. Smears show a few Gram-negative extracellular cocci. Plates show staphylococci and pseudodiphtheria bacilli and a few Gram-negative cocci (gonococci?). Complement fixation test positive.

Case II. Gonorrhea fourteen months ago. Urine after prostatic massage shows scanty mucous sediment with a moderate number of pus cells. Smears show Gram-negative and Gram-positive bacilli, Gram-positive cocci and very few Gram-negative cocci. Plates show Gram-negative bacilli, staphylococci, and streptococci. Complement fixation test positive.

Case III. Gonorrhea five years ago. Urine after prostatic massage shows moderate number of pus cells and a few Gram-negative extracellular cocci. Plates contaminated. Complement fixation test positive.

Case IV. Gonorrhea three years ago. Urine after prostatic massage, shows slight mucous sediment, few pus cells, and a few atypical extra-cellular Gram-negative cocci. Plates sterile. Complement fixation test negative.

Case V. Gonorrhea three years ago. Urine after prostatic massage shows moderate number of pus cells. Smears show many Gram-positive cocci and a few Gram-negative extra- and intra-cellular diplococci. No Gram-negative cocci. Complement fixation test positive.

3. Gonococci negative, both in smear and culture. Nine cases giving a history of gonococcus infection from nine months to fifteen years previously were negative by the complement fixation test thus agreeing with the bacteriological examination. Two cases gave a positive complement fixation test.

Case I. Gonorrhea one year ago. Urine after prostatic massage shows a moderate number of pus cells. Smear shows Gram-positive cocci. No Gram-negative cocci. Plates show staphylococci and streptococci. No Gram-negative cocci.

Case II. Gonorrhea three months ago. Urine after prostatic massage shows few pus cells. Smears show Gram-positive cocci and Gram-negative bacilli. Plates show streptococci and Gram-negative bacilli. In this case the positive complement fixation test was very possibly a fading reaction.

4. Gonococci negative in smear only, cultural examination not made. Six cases, giving a history of gonococcus infection from seven months to five years previously were also negative by the complement fixation test. One case, giving a history of gonococcus

infection two years previously, was positive by the complement fixation test.

5. Cases in which gonococci were not searched for. These cases all had symptoms of chronic urethritis believed to be postgonorrheal. The duration of the urethritis varied from two to fifteen years. Thirty-one cases were examined, of which 10 or 32.2 per cent. gave a positive reaction.

The cases included in groups 2, 3, 4, and 5, were all regarded clinically as postgonorrheal. If now we group all these cases together, we find that out of 54 cases examined a positive result was obtained in 17 or 31.4 per cent. These figures closely correspond with those reported by Keyes¹¹ in postgonorrheal urethritis, in 26 cases carefully examined by smear and culture gonococci were found in 8 or 30.7 per cent. In a number of our cases, however, the result of smear and cultural examinations was suspicious, but inconclusive, as cited in group 2, whereas the complement fixation test was definitely positive or negative. Herein, in our opinion, lies one great advantage of the complement fixation test.

III. VERUMONTANUM DISEASE. GONOCOCCI NOT FOUND.

Twenty-two cases of disease of the verumontanum have been examined. Of these, 21 admitted gonorrhea from one to ten years previously. Four of the 21 gave a positive reaction and 17 a negative reaction. One case, cited in our previous paper, absolutely denied gonorrhea, but had given a positive result on two separate occasions. After six months' treatment he was found to be negative.

IV. CHRONIC PROSTATITIS

1. Gonococci present: Three cases were examined, all of which gave a positive complement fixation test.

2. Cases giving a definite history of gonorrhea—gonococci not searched for.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
5 weeks to 1 year ago	31	20	11
2 years ago	19	9	10
3 years ago	12	5	7
4 years ago	5	2	3
5 years ago	7	0	7
6 years ago	3	2	1
7 years ago	5	2	3
8 years ago	2	1	1
10 years ago	3	1	2
12 years ago	6	3	3
14 years ago	1	0	1
20 years ago	3	1	2
30 years ago	1	0	1
3. Gonorrheal history doubtful	9	2	7
4. Gonorrhea denied	2	0	2

¹¹ Loc. cit.

In group 2 we have a total of 98 cases of chronic prostatitis in which a definite gonorrheal history was obtained. Of these, 46, or 46.9 per cent., gave a positive reaction.

It will be noted that we have obtained positive results in cases where the last gonorrheal infection was stated to be anywhere from six to twenty years ago. We, of course, do not vouch for the accuracy of the patients' statements in that regard. Opinions vary greatly as to the length of time the gonococcus may persist in the genito-urinary organs of the male and female. We feel that a patient giving a positive complement fixation test should be looked upon as still harboring gonococci irrespective of the date of the last gonorrheal infection.

V. SEMINAL VESICULITIS.

Date of last gonorrhea.	No. of cases.	Positive.	Negative.
6 months ago	1	0	1
2 years ago	3	1	2

VI. CLINICALLY CURED CASES.

In this group we have included only such cases as have been looked upon as clinically cured for at least three months. This was done so as to avoid the possibility of including cases which actually were cured but might still present a fading reaction.

We have examined in all 165 cases, of which 22, or 13.2 per cent., gave a positive reaction. These figures correspond closely with those reported by Schmidt¹² at a recent meeting of the American Urological Society. Out of 42 cases examined he obtained a positive result in 5, or 11.9 per cent. Keyes¹³ estimates about 4 per cent. of clinical error in cases apparently cured, basing this statement on the results of laboratory investigation of 86 patients clinically cured of urethral gonorrhea. Thirty-six of his cases were examined by the complement fixation test, and 77 by smear and culture.

In our previous paper we reported 43 per cent. of positive results in cases of this group. Our first series contained all cases examined from the very beginning of the investigation, before we had any definite idea of the possibilities of the test and cases were classed as clinically cured which more rigid examination would probably have excluded from that group. The cases here reported have all been very thoroughly examined before being classed as clinically cured and we think that 13.2 per cent. represents fairly accurately the clinical error in such cases. The importance of these results when the question of marriage arises needs no emphasis here.

¹² Jour. Amer. Med. Assoc., April 27, 1912, p. 1307.

¹³ Loc. cit.

VII. WOMEN.

The diagnosis of gonococcus infection in women is well known to be very difficult and uncertain, and bacteriological methods of diagnosis are not of any great assistance, except in the acute forms which are relatively rare. In subacute and chronic forms, gonococci are generally very scanty. They are to be found more particularly in the discharge from the urethra and cervix. However, the great number and variety of other organisms present in such discharges renders the absolute demonstration of the gonococcus exceedingly difficult both in smear and culture. Very often both clinical and bacteriological examinations leave one in doubt and the diagnosis of chronic gonococcus infection must be only a probable one. Hence, we feel that in women the complement fixation test should prove a distinct addition to our means of diagnosing chronic gonococcus infection.

EXTENT OF INVOLVEMENT NECESSARY TO OBTAIN A POSITIVE REACTION. It will be remembered that in discussing the question of gonococcus infection in the male, it was stated that a positive reaction was not to be obtained if the disease remained confined to the anterior urethra. There had to be at least some involvement of the posterior urethra in order to obtain a positive reaction. In gonococcus infection in the female, the organs chiefly involved are the urethra and Skene's glands, Bartholin's glands, the cervix, the uterine tubes, ovaries, and peritoneum. The vagina very commonly escapes, especially in the adult. In children the vaginal mucosa is much more likely to be infected, as in the young, the pavement epithelium is softer and more like columnar epithelium. Hence, the frequency of gonococcus vulvovaginitis in children.

We have obtained positive reactions in cases of peritonitis, in tuboövarian disease, and in disease of the cervix.

We have also obtained a positive reaction in 2 cases of vulvovaginal abscess, but in the absence of abscess formation, we doubt if a positive reaction will be obtained unless there is some infection of the cervix. In other words, we think a negative reaction will probably be obtained if the disease is limited to the urethra, Skene's glands, and Bartholin's glands. Such cases are doubtless rare, as in the great majority of cases of chronic gonorrhea in the female the cervix is involved. Still we feel that the possibility deserves mention here. In gonococcus infection in young children, the vulva, urethra, and vagina are chiefly affected; only rarely are the cervix, corpus uteri, and tubes involved. We have examined 10 cases of vulvovaginitis in children aged under five years. In all the gonococcus was demonstrated in smear and culture. In all the complement fixation test was negative. This tends to support our opinion that a positive complement fixation will not be obtained unless there is involvement of the cervix.

The important role which the gonococcus plays in the production of pelvic disease in women, scarcely needs mention. Destructive inflammation of the tubes and ovaries, with peritonitis, is common, as is also gonococcus infection of the bladder with secondary ascending infection of the ureters and kidneys.

Finally, on every general maternity service cases of gonorrheal ophthalmia occur from time to time. Statistics show that even with the use of silver nitrate in the eyes, this disease occurs as often as once in every 200 cases. Apart from the possible serious effects upon the eyes of the child itself, there is always great danger of the infection spreading to other infants and nurses. Therefore, on account of the unreliability of the smear and cultural methods of diagnosis of subacute and chronic gonococcus infections in women, we think that the complement fixation test should find a distinct place in gynecological conditions, and that on general maternity services it will be of use in the prevention of gonorrheal ophthalmia.

We have not applied the test as extensively in diseases of the genito-urinary tract in the female as we have in the male. This was principally on account of the fact that our chief object was to study the possibilities and limitations of the test. This could be done much more satisfactorily in the male because the course and development of gonococcus infection is much more readily studied in the male. Furthermore, the complement fixation test could be more thoroughly controlled by bacteriological examination in the male than in the female.

The statistics which follow give, however, a fair idea of the field of usefulness of the complement fixation test in gynecological conditions.

Clinical diagnosis.	Positive.	Negative.
Urethritis and endocervicitis:		
(a) Gonococci present	9	0
(b) Gonococci not found	8	3
Gonorrhea clinically cured	1	4
Chronic gonorrhea, gonococci not found	2	0
Gonorrheal vulvovaginitis; girls under five years, gonococci present	0	10
Salpingo-oöphoritis	9	3
Pyelitis clinically considered gonorrheal	2	6
Vulvovaginal abscess; gonorrheal	2	0
Pelvic peritonitis	3	1
Pregnancy; gonococci present	1	0
Pregnancy; gonococci not found	14	10
Miscellaneous cases from the clinic; lacerations, displacements, etc.	13	50
Pyosalpinx	3	4
Pelvic abscess	0	2

One case clinically diagnosticated as pyosalpinx, and giving a negative complement fixation test, was found at operation to be a case of cystic ovary with normal tubes.

One case diagnosticated as pelvic abscess, and giving a negative

complement fixation test, was found at operation to be a tubo-ovarian abscess from which the colon bacillus was obtained in pure culture.

1. CONCLUSIONS. A positive reaction denotes the presence or recent activity in the body of a focus of living gonococci.

2. A negative reaction does not exclude gonococcus infection but, for the reasons stated, should be accorded considerable importance.

3. A strong positive reaction is not to be expected earlier than about the fourth week, and then only in very acute cases with some complication.

4. A positive reaction is not obtained if the disease is limited to the anterior urethra.

5. A positive reaction does not entirely disappear until seven or eight weeks after cure.

6. In other words, if a strong positive reaction is obtained seven or eight weeks after apparent clinical cure, the patient should be looked upon as still harboring gonococci.

7. In chronic cases, isolation of the gonococcus in culture is the only absolute, bacteriological proof of gonococcus infection.

8. The technique of a complement fixation test is simpler than that of isolation of the gonococcus in culture and the possibilities of error are less.

9. In cases regarded clinically as postgonorrheal, a positive reaction is obtained in 31.4 per cent.

10. In 62 cases of chronic prostatitis giving a history of gonococcus infection within three years, a positive reaction was obtained in 54.8 per cent.

11. In 165 cases looked upon as clinically cured for at least three months, a positive reaction was obtained in 13.2 per cent.

12. In women, a positive reaction is probably not obtained unless there is at least some involvement of the cervix.

13. On account of the unreliability of the bacteriological diagnosis of gonococcus infection in women, the complement fixation test should prove of special usefulness in gynecological conditions.

NOTE.—Since this paper was written, other articles on the subject have appeared, as follows: Smith, *Lancet-Clinic*, Aug. 3, 1912; O'Neil, *Boston Med. and Surg. Jour.*, Oct. 3, 1912; Gardner and Clowes, *New York Med. Jour.*, Oct. 12, 1912. These articles also corroborate the results of previous workers.